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MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

| EXAMINER | |
|---|---|
| TUCKER, ZACHARY C | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/581,412 | BURNS ET AL. | |
| | Examiner | Art Unit | |
| | Zachary C. Tucker | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5,7-10 and 12-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *18* is/are allowed.

6)☒ Claim(s) *1-5,7-10 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10Sep07,26Sep06*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Art Unit: 1624

## DETAILED ACTION

### *Obviousness-Type Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 7-10 and 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 11/397,982. Although the conflicting claims are not identical, they are not patentably distinct from each other because a compound according to instant claims 1 and 3, wherein D is a benzopyrazole-containing heterocyclic ring, is obvious in view of the compounds according to claims 1-8 of the copending application. Note the compounds whose structure is diagrammed in instant claim 3 at the point bridging pages 9 and 10 of the Preliminary Amendment filed in the instant application 1 June 2006 (this is a duplicate structure; a rejection under 35 U.S.C. 112, second paragraph appears *infra*, based on this

deficiency in the claims). Instant claims 1 and 3 are overlapping in scope with claims 1-8 of the copending application.

Since instant claim 7 specifies a composition comprising a compound according to instant claim 3, claim a composition according to copending claim 9 renders instant claim 7 obvious as well.

Since instant claims 8-10 and 12 specify a method of treating a protein kinase-associated disease state, comprising administering a therapeutically effective amount of a compound according to instant claim 3, copending claims 10-16, which specify a method of treating a protein kinase-associated disease state, comprising administering a compound according to copending claim 1, render those claims obvious, because the compound according to copending claim 1 is overlapping with instant claim 3.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 8-10 and 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 11/711,957. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 3, from which instant claims 8-10 and 12 depend, are overlapping in scope with the formula specified in the method according to claim 1 of the copending application.

Limitations specified in instant claims 8-10 and 12 correspond with limitations specified in copending claims 4, 6 and 7.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Art Unit: 1624

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first and second paragraphs of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 5 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the synthesis of compounds of general formula (I) and the hydrates thereof and pharmaceutically acceptable salts thereof, does not reasonably provide enablement for the full scope of prodrugs of a compound of formula (I) and all solvates and crystal forms of a compound of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Wands factors provide a guide for determining the scope of enablement provided by a given disclosure:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.
*In re Wands*, 858 F.2d 731,737 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

Each will be addressed, with respect to the solvates embodiment "prodrugs... thereof" and "solvates, crystal forms thereof" embodiments.

*Prodrugs Are Not Enabled*:

(A) Though it might appear that the scope of instant claims 1, 2, 4, 5 and 13-17 is limited to compounds of formula (I) having the structure depicted, it is not. A prodrug, as defined by Bundgaard in:

Hans Bundgaard, Design of Prodrugs, page 1. © 1985 Elsevier Science Publishers.

"is an inactive species, and therefore, once its job is completed, intact prodrug represents unavailable drug." Thus, an important requirement of prodrugs of compounds having the formula (I) is that they be pharmacologically inactive. Prodrugs come in myriad forms, and are not limited to only ester and amide derivatives, which are most commonly cited as examples, and suggested as the preferred type of prodrug on page 15 of the instant specification. A prodrug may also be a Mannich base (imine), an acyclic precursor to a cyclic compound, a polymer-bound drug (either covalently or ionically), a compound of the drug covalently or ionically bound to another drug with different action or a carboxylic acid which is decarboxylated to provide the active drug.

So, the scope of all prodrugs is quite broad. A prodrug does not depend on the identity of the pharmacologically active agent formed from the prodrug for patentability. A prodrug is not necessarily even structurally related to the compound of which it is a prodrug, since the metabolism *in vivo* of that compound is what provides the drug.

(B) Prodrugs of a compound having the formula (I) are the nature of the invention. These are chemical compounds.

(C) The state of the prior art with respect to the development of prodrugs is represented by:

> Richard B. Silverman, The Organic Chemistry of Drug Design and Drug Action, pages 352-400. © 1992 Academic Press, Inc.

Silverman teaches many kinds of prodrugs, including all of the types mentioned above in section "(A)." Pages 353 and 354 list eight various reasons why a prodrug would be desirable. On page 354, Silverman teaches that some prodrugs are discovered accidentally, and some designed on the basis of known metabolic transformations.

(D) The level of ordinary skill in the art is that of a medicinal chemist, holding a graduate level degree in the field and with experience in preparative organic chemistry.

(E) As discovery of prodrugs is sometimes accidental, then it follows that whether a given compound will function as a prodrug or not is sometimes unpredictable. On the other hand, when a compound is designed as a prodrug, one must first understand the metabolic milieu into which the presumptive prodrug is to be introduced, and must also know to what extent the compound will be metabolized. The metabolism of xenobiotics is not always predictable. A prodrug must also, by definition, be pharmacologically inactive, so one must know which modifications of the structure of the parent compound will render it inactive. Structure-activity relationships must in large part be determined empirically, although once a rule is discerned, the structure-activity of a given series of compounds becomes predictable.

Theoretically, if one of ordinary skill in the art knew all of the above variables, prodrug structure could be predicted in advance. The reality is that all of these

considerations, in total, must be empirically devised when the compound in question is a novel compound, as is the compound having formula (I).

(F) The direction given in the instant specification which pertains to the production of prodrugs of formula (I) compounds appears at page 15, lines 3-19. No metabolic studies of the compounds *in vivo* have been done and no structure-activity rules are outlined – certainly no teaching as to which modifications will afford an *inactive* compound is found in the specification. The specification does not specifically address any type of prodrug other than amides (amino acid-derivatized amides) and carboxylate esters at page 15.

(G) No working examples of a prodrug are in the disclosure.

(H) In order for one of ordinary skill in the art to practice the full scope of the prodrugs of compounds having the formula (I), a complete structure activity analysis would have to be completed. The practitioner would first screen for which type of modifications of the molecular structure would render an inactive compound. Then, the metabolic studies of all of the inactive compounds would have to be completed, and compounds that are converted to active compounds of formula (I) *in vivo* identified. This research would potentially be inconclusive and could take years. Additionally, one of ordinary skill in the art would necessarily have to undertake an effort to make totally new compounds not bearing any structural similarity to the compounds having the formula (I), such as the procyclic compounds converted to heterocyclic compounds *in vivo*, which are mentioned on page 360 of Silverman. Work with polymeric forms of the compounds having formula (I) would be necessary also. Because different animals' metabolisms differ to the extent that xenobiotics are handled by different enzymatic pathways, this effort would have to be

duplicated in each species for which a prodrug were sought. As evidence that animals will differ substantially in the manner that xenobiotics are metabolized, the examiner presents:

> Al-Dabbagh and Smith, "Species differences in oxidative drug metabolism: some basic considerations." Archives of toxicology. Supplement. Archiv fur Toxikologie. supplement, vol. 7, pages 219-231 (1984).

Al-Dabbagh and Smith teaches that the metabolic process itself is highly variable both between and within animal species, and that the toxic effect of many chemicals is a function of how the chemical is metabolized rather than the substance itself.

Given the amount of direction in the disclosure, this amount of experimentation is clearly undue. Applicants have not described manner and process of making prodrugs of compounds having the formula (I), in such full, clear, concise, and exact terms as to enable any person skilled in the art to do so.

*Solvates Are Not Enabled*:

(A) Insofar as the solvate embodiment of claims 1, 2, 4, 5 and 13-17 is concerned, those claims read on solvates of compounds according to formula (I). The scope of the solvates recited in the claims includes solvates of a compound according to formula (I), with *any* solvent. The definition of a solvate, taken from the Vippagunta et al reference, cited in section (C), (D), (E) below, is a "crystalline solid adduct[s] containing solvent molecules within the crystal structure, in either stoichiometric or nonstoichiometric proportions, giving rise to unique differences in the physical and pharmaceutical properties of the drug."

(B) The nature of the invention is that of a chemical compound, a pharmaceutical composition or a medical treatment method.

(C), (D), (E) Solvates, at the time the invention was made, were known, but not to such an extent that the preparation of those solvates other than hydrates was routine or simple. The following references address the state of the art with respect to crystalline forms of organic compounds, formation of solvates of organic compounds, and the predictability thereof.

> Vippagunta et al, "Crystalline Solids" Advanced Drug Delivery Reviews, vol. 48, pages 3-26 (2001).
>
> and
>
> Gavezzotti, "Are Crystal Structures Predictable?" Accounts of Chemical Research, vol. 27, pages 309-314 (1994).

First, it is evident from both of the references that formation of specific crystalline forms, and more particularly, solvates, is highly unpredictable. See Gavezzotti, page 312, point #8, and Vippagunta et al, page 11, "Prediction of Polymorphs" and page 18 "Prediction of the formation of hydrates and solvates."

Because the formation of solvates is unpredictable, even the relatively high level of skill possessed by one of ordinary skill in the art is not enough to render preparation of solvates routine. Each solvate of each compound must be experimentally prepared (since the conditions necessary for the formation cannot be predicted), wherein all of the factors relevant to each individual compound's ability to crystallize and form solvates are studied. These factors are identified in points #1-7 of the Gavezzotti reference. The preparation of each single claimed solvate represents a significant undertaking in the areas of preparative organic chemistry, physical chemistry, and crystallographic measurements.

It is unknown that the full scope of solvates of compounds of formula (I) is even possible (see Gavezzotti, page 309, point #1).

(F) The disclosure includes no guidance for making the claimed solvates of formula (I) compounds.

(G) No working examples demonstrate preparation of a solvate. In fact, compounds of the invention are crystallized from a variety of solvents throughout the working examples, yet no solvate is identified.

(H) Each compound of formula (I), of which there are thousands, as a solvate with every solvent within the scope of "solvate" generally, of which there are also thousands, represents the efforts of many over a period of years. Those efforts are potentially inconclusive. For one of ordinary skill in the art to conduct the type of research outlined in Gavezzotti and in Vippagunta et al for preparation of every one of the claimed solvates would be undue. Applicants' right to exclude others from making all solvates of compounds according to formula (I) is unwarranted in light of the lack of any direction as to how one of ordinary skill would do so.

*Crystal Forms Are Not Enabled*:

(A) Insofar as the "crystal forms" embodiment of the instant claims is concerned, the claims include *any* crystal form, any polymorph, that is, of a formula (I) compound.

(B) The nature of the invention is that of a special physical form of a formula (I) compound.

(C) The state of the art with respect to the "crystal forms" embodiment of instant claims 1, 2, 4, 5 and 13-17 is well-characterized by the Gavezzotti and Vippagunta et al references, cited hereinabove in the rejection of claims 1, 2, 5 and 13-17 under the first paragraph of this statute, for lack of enablement of the claimed solvates of formula (I) compounds.

(D) The level of ordinary skill with respect to the "crystal forms" embodiment of instant claims 1, 2, 4, 5 and 13-17 is that of a preparative organic chemist, with experience preparing and identifying crystalline forms of chemical compounds.

(E) It is evident from both of the references that formation of specific crystalline forms is highly unpredictable. See Gavezzotti, page 312, point #8, and Vippagunta et al, page 11, "Prediction of Polymorphs" and page 18 "Prediction of the formation of hydrates and solvates."

(F) The instant specification does not provide any guidance relevant to the preparation of special "crystal forms" of formula (I) compounds according to the present invention.

(G) There are no working examples of any "crystal forms" of formula (I) according to the present invention.

(H) Given the above facts, it can be concluded that the instant specification does not provide the requisite level of enablement with respect to the claimed "crystal forms," in general, of formula I compounds. In order to practice the invention according to instant claims 1, 2, 4, 5, and 13-17 commensurate in scope with those claims, one of ordinary skill would have to labor for years, crystallizing formula (I) compounds, and measuring the crystal structure of each putative crystal form thereof (such as by powder X-ray diffraction).

Claims 8-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 8-10 and 12 are drawn to a method of treating a protein kinase-associated disease state, comprising administering a therapeutically effective amount of at least one compound of claim 1, to a subject in need thereof.

The compounds of the invention are shown to have activity only in the inhibition of some Janus kinases ("JAK's"), and evidence of the compounds' activity inhibiting other types of kinases recited in the claims is not provided in the disclosure. Thus, those diseases which are "associated" with a kinase other than JAK kinases are not treatable with compounds of the present invention.

Claims 8-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of leukemia and lymphoma, does not reasonably provide enablement for treatment of the other diseases recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Wands factors will be addressed with respect to the methods claimed in claims 8-10 and 12:

(A) The claims are drawn to treatment of a wide variety of medical conditions/diseases, such as atopy, a cell –mediated hypersensitivity, a rheumatic disease, an autoimmune disease, a viral disease. a neurodegenerative disease, a cardiovascular disease, and a cancer. This terminology includes all cancers, all viral diseases, all forms of autoimmune diseases, all forms of rheumatic diseases, all forms of cell-mediated hypersensitivity, all neurodegenerative diseases, all forms of cardiovascular diseases, and all forms of atopy.

(B) The nature of the invention claimed in claims 8-10 and 12 is a medical treatment method.

(C) The state of the art with respect to the therapeutic application of inhibitors of Janus kinases (JAKs), is well –characterized by the following reference:

> Duhé et al, "Negative Regulation of Janus Kinases" *Cell Biochemistry and Biophysics*, vol. 34(1), pages 17-59 (2001).

Duhé teaches that inhibitors of JAKs have activity against lymphoma/leukemia cells (page 46, last paragraph in column one), and against type I hypersensitivity reactions (page 48, first paragraph in column one), but notes in the concluding remarks that

> "...much work remains to be done to precisely determine the functional relevance of JAKs in signaling pathways initiated through the angiotensin II $AT_1$ receptor , the IgE Fcξ receptor and perhaps through other receptor systems. In the challenging discipline of signal transductions, it is all too easy to confuse biochemical correlations with causality, and the current state of knowledge is limited by ignorance of other signal components. With the recent generation of transgenic animals deficient in specific JAKs and STATs, with the discovery of new signal transduction components such as the SOCS proteins, and with the development of increasingly selective inhibitors such as WHI-P131, knowledge of JAKs becomes ever more refined. Indeed, such knowledge must be as precise and accurate as possible to achieve the goal of alleviating human disease through JAK-targeted pharmacological therapy."

It is therefore evident that the state of the art at the time the invention was made was not such that the full scope of instant claims 8-10 and 12 was practicable by one of ordinary skill in the practice of medicine.

(D) The level of ordinary skill with respect to the invention claimed in claims 8-10 and 12 is that of a physician specializing in the treatment of the disease states recited in those claims.

(E) The level of predictability with respect to new medical treatment methods is low. Especially in light of the above-quoted passage from Duhé et al, treatment of diseases by administering an inhibitor of a JAK is not predictable, absent some showing of activity against the disease in an animal or *in vitro* model of it.

(F) The amount of guidance provided in the disclosure with respect to the invention claimed in claims 8-10 and 12 is not extensive, given the breadth of the claimed method,

On page 21 of the instant specification, a suggested dosage range, in the most particular embodiment, is provided as being from 1mg to 1,000mg, preferably once or twice per day. No specific dosages are correlated with any specific disease, however.

At pages 17 (line 28) to 20 (line 24), pharmaceutical compounding direction is provided. This information, however, is well-known to those of ordinary skill in the art of pharmacy.

(G) There are no working examples of a method of claim 8-10 and 12 provided in the disclosure.

(H) Given the paltry amount of direction provided in the disclosure, and the extremely broad scope of diseases specified in claims 8-10 and 12, it would be unwarranted to grant applicants an exclusive right to practice the invention according to those two claims. To practice the invention according to claims 8-10 and 12, one of ordinary skill would necessarily have to determine the effective dosages for each disease within the scope of instant claims 8-10 and 12, and devise methods for testing individual compounds according to formula (I) against those diseases. Because there are literally thousands of compounds embraced by formula (I), and hundreds (at least) of diseases which are "protein kinase-associated," this amount of experimentation is undue.

Claims 1, 2, 4, 5 and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Recitation of "prodrug... thereof" in claims 1 and 2 renders those claims indefinite in scope. Applicants may opine that one of ordinary skill understands what the term "prodrug" means. The examiner is not pretending that one of ordinary skill does not understand what *function* a prodrug serves. This is not the issue here. What is claimed are chemical compounds which serve as prodrugs for the compounds of formula (I). The claim, therefore, is drawn to a group of *molecular structures*, that when subjected to a biological milieu in a live animal, will be metabolically converted to a compound of formula (I). One of ordinary skill cannot possibly be aware of the full scope of all of the different molecular arrangements which will provide the compounds (I) upon being metabolized, in all animals. Page 15 of the specification only provides a few examples of what applicants intend the term to encompass. The only type of prodrug discussed is ester and amide derivatives.

As evidenced by the Al-Dabbagh and Smith reference, cited *supra*, in the rejection of the claimed prodrugs under the first paragraph of 35 U.S.C. 112, animals will differ significantly in the manner that xenobiotics are metabolized. Therefore, a compound that is a prodrug in humans is not necessarily a prodrug in a cat, for example.

Additionally, in claim 1, the recitation "Q is a bond" renders it impossible for formula (I) compounds to possess the bonding arrangement shown in formula I. Specifically, when "Q" is a bond, "W" cannot be present. There is no reference to the status of "W" when "Q" is a bond anywhere in the claim. This renders claim 1 further indefinite.

Claim 5 is further indefinite, in addition to being indefinite for depending from an indefinite base claim, because the limitation "or a pharmaceutically acceptable prodrug, salt, hydrate, crystal form, or diastereomer thereof" lacks antecedent basis in claim 3, from which it depends. Claim 5 has been examined on the merits as though this limitation found antecedent basis in the claim.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The molecular structure diagram appearing at the point bridging pages 9 and 10 of the Preliminary Amendment filed 1 June 2006 is duplicated. Deletion of one of the occurrences of this molecular structure diagram is recommended. Repetition of Markush group members renders a claim indefinite, because it is not clear whether some different Markush group member was intended in place of the repeated member.

***Allowable Subject Matter***

Terminal disclaimers disclaiming the terminal part of any patent granted on copending Application Nos. 11/397,982 and 11/711,957 would overcome the Obviousness-Type Double Patenting rejections of claims 1, 2, 7-10 and 12 set forth herein.

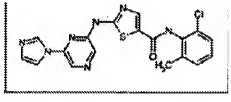
Amendment of claims 8 and 10-12 to limit the scope of the methods according to the instant claims to treatment of only leukemia or lymphoma (as taught at page 5 in Table 1 and page 16, line 6, of the instant specification) would overcome the rejection of those claims under the first paragraph of 35 U.S.C. 112.

Deletion of all reference to "prodrugs," "solvates" and "crystal forms" in claims 1 and 2 will overcome the rejections under 35 U.S.C. 112, first and second paragraphs of claims 1, 2, 4, 5 and 13-17.

Deletion of the Markush group member appearing in claim 3, at the point bridging pages 9 and 10 of the Preliminary Amendment filed 1 June 2006, will overcome the rejection of that claim under 35 U.S.C. 112, second paragraph.

Claim 18 is allowed.

No disclosure of, nor any teaching which renders obvious the compounds according to claims 1-5 or 13-18 was found in a search of the prior art. The closest prior art with respect to the compounds according to claims 1-5 and 13-18 is WO 00/62778 (Das et al), cited in the Information Disclosure Statement filed 26 September 2006, which discloses, at page 165, a compound having the structure represented by the following diagram:



which bears a superficial similarity to compounds according to instant claim 1, except for the fact that "D" may not be imidazol-1-yl in instant claims 1-5 and 13-18.

***Conclusion***

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 9:00am to 5:00pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Art Unit: 1624

/Zachary C. Tucker/
Primary Examiner
Art Unit 1624